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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,581	05/14/2001	Nabil Hanna	P 0280617 1997-30-0568A	7197

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/853,581	HANNA ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-46 and 49-64* is/are rejected.

7)☒ Claim(s) *47 and 48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Hanna *et al.*

Date of priority: September 18, 1997

Response to Amendment

The Amendment filed September 24, 2004 in response to the Office Action of March 24, 2004 is acknowledged and has been entered.

Claims 1-43 were cancelled.

New claims 44-64 were added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

New Claim Objections:

Claim 52 is object to for reciting "the method of claim 52" which depends from itself. It is assumed, for examination purposes, that claim 52 limits the subject matter of Claim 51.

New Claim Rejections:

Claims 53, 57, and 62 are rejected under 35 USC 112, 2nd paragraph for the recitation of specific trademarks MPEP 2173.05 (u). The scope of the claims is uncertain since the trademarks cannot be used properly to identify any particular material or product.

Claims 63-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case *only* sets forth an admixture that does not contain muramyl dipeptide or an admixture that contains no more than 20 micrograms of muramyl dipeptide (MDP). Thus, the written description is not commensurate in scope with the claims drawn to an antigen-containing admixture that contains no more than 20 micrograms of any immunostimulating peptide and or wherein the antigen-containing admixture lacks any immunostimulating peptide.

The specification teaches (page 12, lines 9+) the importance that a peptide component, especially a muramyl dipeptide (MDP) be lacking from the claimed antigen formulation because such a peptide will interfere with induction of a CTL response if it provided in an amount greater than about 20 micrograms. However, the specification is silent on what other immunostimulatory peptides should be present and or absent in any amounts. Thus, there is incomplete evidence of possession and or contemplation of a genus of immunostimulatory peptides that should be absent from the admixture and a lack of a written description of other qualifying immunostimulatory peptides.

The instant disclosure of a single species of muramyl dipeptide fails to adequately describe the scope of the claimed genus of immunostimulants. Under the written description guidelines, a description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features

common to the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of immunostimulatory peptides that encompass the genus nor does it provide a description of structural features that are common to these immunostimulatory peptides. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of one species is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at

page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of immunostimulatory peptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Rejection Maintained:

Claims 44-46, 49-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raychaudhuri *et al.* (US Patent No. 5,695,770, June 1995, IDS) in combination with the teachings of Patent Application No. 2002/0004052 A1 (BERD *et al.*, June 7, 1995) and Berd *et al.* (Cancer Research, Vol. 46, May 1986, pages 2572-2577) for the reasons of record as previously applied to claims 23-26, 29, 38-43.

It should be noted that new claims 51-64 are anticipated by Raychaudhuri et al., US Patent No. 5,695,770, June 1995, IDS—see entire article.

Applicants appear to argue that the prior art of Berd *et al.* does not describe nor suggest the admixture *in combination* with a therapeutically effective amount of at least one agent which is capable of neutralizing, blocking, antagonizing, or down regulating the activity or preventing activation of TGFβ. This argument has been considered but is not found persuasive. As set forth previously, Berd *et al.* taught the administration of an antagonist of an immunosuppressive factor administered sequentially or concurrently, and in any order with the adjuvant composition wherein said antagonist was cyclophosphamide. Furthermore, as set forth previously, it was shown that low dose cyclophosphamide "is capable of" neutralizing, blocking, antagonizing, or down regulating the activity or preventing activation of TGF-β. Applicants argue that one of skill in the art would not consider the "effects" of cyclophosphamide (CY) on TGFβ to be so clear-cut. Applicants counter that the abstracts of Takiguchi *et al.*, Lian *et al.* and Weiner *et al* reveal that CY does not effect the amount of TGF-β mRNA and or increases TGFβ expression. This argument has been considered but is not found persuasive. The abstract of Takiguchi *et al.* only teaches that that there was no observable increase in TGFβ mRNA following the treatment of CY *and* another cytokine, TNF. This says nothing about the capability of CY alone to neutralize, block, antagonize, down regulate, or prevent the activation of TGFβ in tumor bearing animals. Further, the references of Lian *et al.* and Weiner *et al.* are nonanalogous because they don't consider the effects of CY in tumor bearing mammals. Weiner *et al.* is concerned with the treatment of multiple sclerosis, while Lian *et al.* is concerned with expression of TGFβ in the developing brain of normal and diabetic mouse embryos. Furthermore, the abstracts of Weiner *et al.* and Lian *et al.* are silent with regards to the dosage of CY that effects TGFβ production. Applicants also refer to a later abstract published by Matar *et al.* and add that the teachings of

such abstract make it clear that the effect of CY treatment on cytokine expression that Matar *et al.* consider to be significant with regard to immunopotentiation is a reduction in T-cell derived IL-10 production, "rather than any effect on TGFβ production or activity". This argument has been considered but is not found relevant. What Matar *et al.* considers to be significant with regards to immunopotentiation says nothing about the direct or indirect effects of CY on TGF-β. On the contrary, the abstract teaches that the treatment of low CY reduced the splenic production of these suppressive cytokines, inlcluding TGF-β. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

Claims 47-48 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN

GARY NICKOL
PRIMARY EXAMINER